

## REMARKS AND ARGUMENTS

The Office Action states that claims 14-19 are under examination and claims 1-13 and 20-26 have been withdrawn from consideration. However, based on the telephone conference with the Examiner held on September 5, 2003, Applicants request that claims 6-13 be examined at this time. Accordingly, claims 1-5 and 14-26 have been withdrawn herein with the understanding that the claims defining methods (claims 20-23) and devices (claims 14-19) will be rejoined when the pending claims are allowed. Claim 6 has been amended to better claim the subject matter which Applicants regard as the invention and for improved clarity. No new matter had been added in this Amendment.

### Claim Rejection under 35 U.S.C. § 103:

Claim 14 is rejected under 35 U.S.C. § 103 as allegedly unpatentable over Colvin (United States Patent No. 6,344,360) or Balbo (United States Patent No. 5,061,626). This rejection applies to claim 6 with the entry of this Amendment. Applicants respectfully traverse this rejection.

The Office Action states that both Colvin and Balbo disclose polylysine itself as a solid phase support and suggest that additional groups can be attached to the polylysine. The Office Action further states that the requirements of claim 6 are met if a reference discloses peptides (which can be linear) which are bonded to a solid phase support, which peptides contain at least one lysine, and with the further requirement that all such peptides do not have the same molecular weight.

With the entry of this Amendment, amended claim 6 defines an endotoxin removal adsorbent comprising a ligand immobilized on a solid phase support medium, the ligand consisting essentially of a mixture of oligopeptides, of which at least one oligopeptide is a

branched oligopeptide, said oligopeptides being composed of one or more amino acids having a  $pK > 7.2$ , said oligopeptides being polydisperse with respect to molecular weight and to number of branches per molecule.

Applicants submit that the claimed invention is distinct from the teachings of the cited patents. Applicants further argue that there is no suggestion of the invention in the cited patents. The invention is directed to an adsorbent which utilizes a ligand consisting of a mixture of linear and branched or branched oligopeptides. Furthermore, amended claim 6 specifically recites that the mixture of the oligopeptides be polydisperse with respect to molecular weight and to the number of branches per molecule.

In contrast, the cited patents mention "polylysine" simply as an example of solid support material or linker to which certain reactive groups (e.g.,  $-NH_2$  or  $-OH$ ) can be attached. The term "polylysine" as used in the cited patents refers to a linear homopolymer molecule consisting of the amino acid residue, lysine. There is no mention or suggestion therein of the ligand of the invention, i.e., the mixture of linear and branched or branched oligopeptides exhibiting high degree of polydispersity. Moreover, there is no functional link between polylysine mentioned (as a mere solid support) in Colvin and Balbo, and the ligands herein which show sufficient heterogeneity to effectively adsorb a large variety of endotoxin. Because of this, one of ordinary skill in the art would not have been motivated to make and use the invention based on the teachings of Colvin and Balbo.

Based on the foregoing, Applicants submit that claim 6 is not *prima facie* obvious over Colvin or Balbo. Withdrawal of the rejection of claim 6 is respectfully requested.

Claim 14 is further rejected under 35 U.S.C. § 103 as allegedly unpatentable over Kauvar (United States Patent No. 5,599,901). For the reasons stated above, claim 6 is at issue. Applicants respectfully traverse this rejection.

The Office Action alleges that Kauvar discloses a "family" of peptides which are to be bonded to a solid phase support. For the same reasons alleged above in view of the Colvin or Balbo patents, the Examiner states that claim 6 is rendered obvious in view of Kauvar.

Applicants point out that Kauvar describes certain linear peptides useful in separation and purification of biological materials. There is no mention or suggestion of branched oligopeptides or a mixture of linear and branched oligopeptides composed of one of more amino acids having a  $pK > 7.2$ , which are polydisperse with respect to molecular weight and to number of branches per molecule. There is nothing in Kauvar that would motivate a person of ordinary skill in the art to make and use the invention. Withdrawal of the rejection is respectfully requested.

Claims 14 and 19 (i.e., claims 6 and 13 with the entry of this Amendment) are rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Suzuki (European Patent No. 0,028,937) in view of Carter (United States Patent No. 5,780,594). Applicants respectfully traverse this rejection.

As stated in the Office Action, Suzuki discloses a device for removing noxious substances from blood and the device contains albumin bonded to a solid phase support. Carter discloses the amino acid sequence of human albumin.

Albumin is a linear polypeptide. Neither Suzuki nor Carter teaches or suggests the ligand of the invention which consists of a mixture containing at least one branched oligopeptide and exhibits certain properties as demonstrated in the present application. Nothing in the cited references provide any motivation to a skilled artisan to make and use the claimed invention.

In summary, in view of the arguments and amendments made herein, Applicants submit that the claims are not *prima facie* obvious over the cited patents. Withdrawal of the rejection under 35 U.S.C § 103 is respectfully requested.

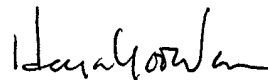
Conclusion:

Based on the foregoing, this case is considered to be in condition for allowance and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone call is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This Amendment is accompanied by a Petition for Extension of Time (two months) and a check in the amount of \$410.00 as required under 37 C.F.R. 1.17(a)(2) for a large entity. However, if the amount submitted is incorrect, please charge any deficiency or credit any overpayment to Deposit Account No. 07-1969.

Respectfully submitted,



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